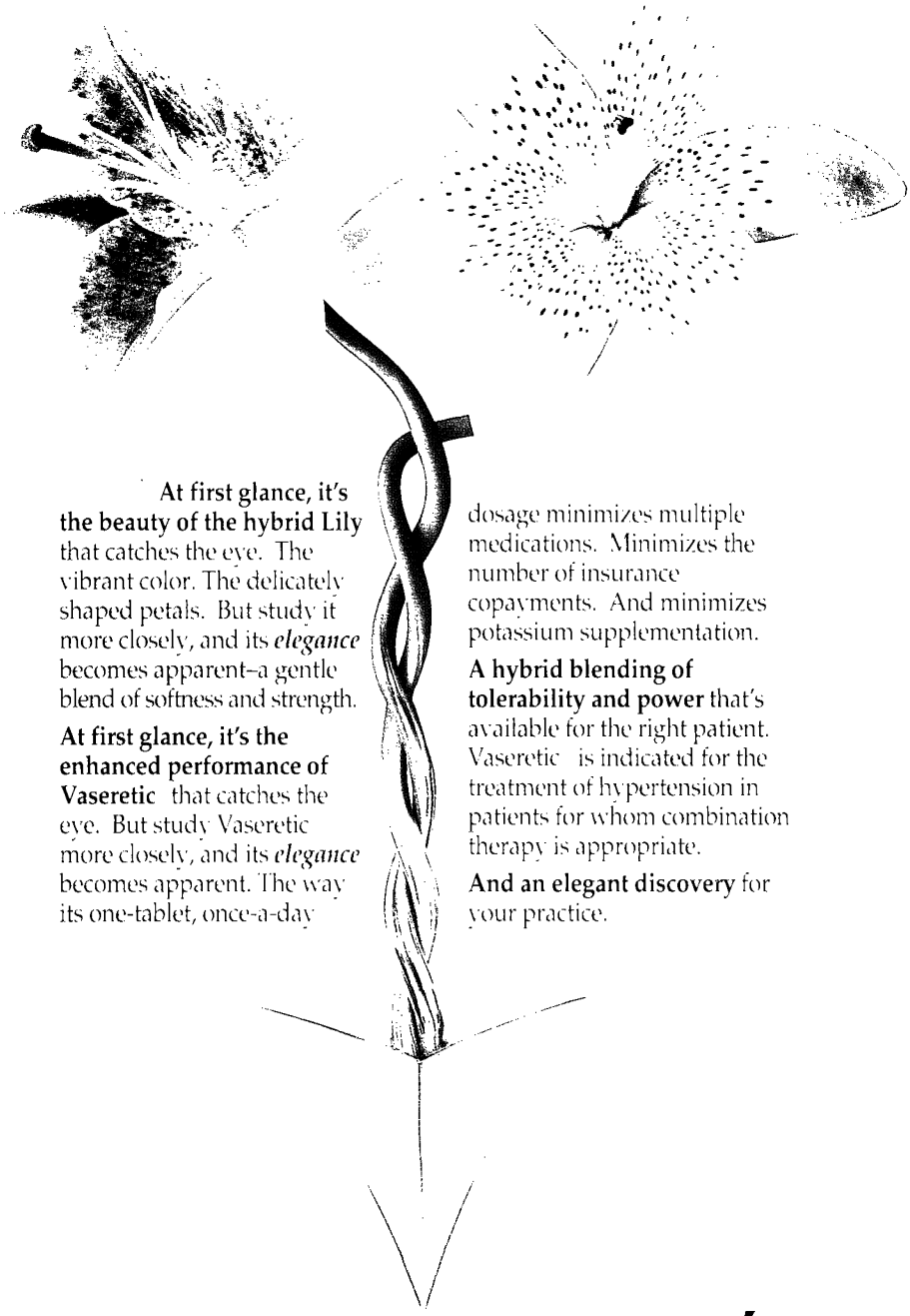
Discover The Elegance Of A Hybrid



At first glance, it's the beauty of the hybrid Lily that catches the eye. The vibrant color. The delicately shaped petals. But study it more closely, and its ***elegance*** becomes apparent–a gentle blend of softness and strength.

At first glance, it's the enhanced performance of Vaseretic that catches the eye. But study Vaseretic more closely, and its ***elegance*** becomes apparent. The way its one-tablet, once-a-day dosage minimizes multiple medications. Minimizes the number of insurance copayments. And minimizes potassium supplementation.

A hybrid blending of tolerability and power that's available for the right patient. Vaseretic® is indicated for the treatment of hypertension in patients for whom combination therapy is appropriate.

And an elegant discovery for your practice.

VASERETIC® 10-25 *Next*

Enalapril Maleate-Hydrochlorothiazide

Vaseretic® is contraindicated in patients who are hypersensitive to any component of this product or to other sulfonamide–derived drugs and in patients with a history of angioedema related to previous treatment with an ACE inhibitor.
Dosage must be individualized; the fixed combination is not for initial therapy.
Evaluation of the hypertensive patient should always include assessment of renal function.
For a Brief Summary of Prescribing Information, see adjacent pages.

USE IN PREGNANCY: When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, Vaseretic (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, *Fetal/Neonatal Morbidity and Mortality.*

TABLETS
VASERETIC®
(ENALAPRIL MALEATE-HYDROCHLOROTHIAZIDE)

USE IN PREGNANCY: When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC® (Enalapril Maleate-Hydrochlorothiazide) should be discontinued as soon as possible. See WARNINGS, *Fetal/Neonatal Morbidity and Mortality*.

CONTRAINDICATIONS: VASERETIC is contraindicated in patients who are hypersensitive to any component of this product and in patients with a history of angioedema related to previous treatment with an angiotensin converting enzyme inhibitor. Because of the hydrochlorothiazide component, this product is contraindicated in patients with anuria or hypersensitivity to other sulfonamide-derived drugs.

WARNINGS: *General; Enalapril Maleate; Hypotension:* Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume depleted persons such as those treated vigorously with diuretics or patients on dialysis.

Syncope has been reported in 1.3 percent of patients receiving VASERETIC. In patients receiving enalapril alone, the incidence of syncope is 0.5 percent. The overall incidence of syncope may be reduced by proper titration of the individual components. (See PRECAUTIONS, *Drug Interactions*, and ADVERSE REACTIONS.)

In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased. Similar considerations may apply to patients with ischemic heart or cerebrovascular disease, in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.

If hypotension occurs, the patient should be placed in the supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which usually can be given without difficulty once the blood pressure has increased after volume expansion.

Angioedema: Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported in patients treated with angiotensin converting enzyme inhibitors, including enalapril. This may occur at any time during treatment. In such cases VASERETIC should be promptly discontinued and appropriate therapy and monitoring should be provided until complete and sustained resolution of signs and symptoms has occurred. In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal. **Where there is involvement of the tongue, glottis or larynx, likely to cause airway obstruction, appropriate therapy, e.g., subcutaneous epinephrine solution 1:1000 (0.3 mL to 0.5 mL) and/or measures necessary to ensure a patent airway, should be promptly provided.** (See ADVERSE REACTIONS.)

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor (see also CONTRAINDICATIONS).

Neutropenia/Agranulocytosis: Another angiotensin converting enzyme inhibitor, captopril, has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Hydrochlorothiazide: Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Lithium generally should not be given with thiazides (see PRECAUTIONS, *Drug Interactions, Enalapril Maleate and Hydrochlorothiazide*).

Pregnancy; Enalapril-Hydrochlorothiazide: There was no teratogenicity in rats given up to 90 mg/kg/day of enalapril (150 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 ½ times the maximum human dose) or in mice given up to 30 mg/kg/day of enalapril (50 times the maximum human dose) in combination with 10 mg/kg/day of hydrochlorothiazide (2 ½ times the maximum human dose). At these doses, fetotoxicity expressed as a decrease in average fetal weight occurred in both species. No fetotoxicity occurred at lower doses; 30/10 mg/kg/day of enalapril-hydrochlorothiazide in rats and 10/10 mg/kg/day of enalapril-hydrochlorothiazide in mice.

When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and even death to the developing fetus. When pregnancy is detected, VASERETIC should be discontinued as soon as possible. (See *Enalapril Maleate, Fetal/Neonatal Morbidity and Mortality*, below.)

Enalapril Maleate; Fetal/Neonatal Morbidity and Mortality: ACE inhibitors can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature. When pregnancy is detected, ACE inhibitors should be discontinued as soon as possible.

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from decreased fetal renal function; oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation, and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to the ACE-inhibitor exposure.

These adverse effects do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to ACE inhibitors only during the first trimester should be so informed. Nonetheless, when patients become pregnant, physicians should make every effort to discontinue the use of VASERETIC as soon as possible.

Rarely (probably less often than once in every thousand pregnancies), no alternative to ACE inhibitors will be found. In these rare cases, the mothers should be apprised of the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intraamniotic environment.

If oligohydramnios is observed, VASERETIC should be discontinued unless it is considered lifesaving for the mother. Contraction stress testing (CST), a non-stress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury.

Infants with histories of *in utero* exposure to ACE inhibitors should be closely observed for hypotension, oliguria, and hyperkalemia. If oliguria occurs, attention should be directed toward support of blood pressure and renal perfusion. Exchange transfusion or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function. Enalapril, which crosses the placenta, has been removed from neonatal circulation by peritoneal dialysis with some clinical benefit, and theoretically may be removed by exchange transfusion, although there is no experience with the latter procedure.

No teratogenic effects of enalapril were seen in studies of pregnant rats and rabbits. On a mg/kg basis, the doses used were up to 333 times (in rats), and 50 times (in rabbits) the maximum recommended human dose.

Hydrochlorothiazide; Teratogenic Effects: Reproduction studies in the rabbit, the mouse and the rat at doses up to 100 mg/kg/day (50 times the human dose) showed no evidence of external abnormalities of the fetus due to hydrochlorothiazide. Hydrochlorothiazide given in a two-litter study in rats at doses of 4 - 5. 6 mg/kg/day (approximately 1 - 2 times the usual daily human dose) did not impair fertility or produce birth abnormalities in the offspring. Thiazides cross the placental barrier and appear in cord blood.

Nonteratogenic Effects: These may include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

PRECAUTIONS: *General; Enalapril Maleate; Impaired Renal Function:* As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients with severe congestive heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with angiotensin converting enzyme inhibitors, including enalapril, may be associated with oliguria and/or progressive azotemia and rarely with acute renal failure and/or death.

In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20 percent of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients renal function should be monitored during the first few weeks of therapy.

Some patients with hypertension or heart failure with no apparent pre-existing renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when enalapril has been given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction of enalapril and/or discontinuation of the diuretic may be required.

Evaluation of the hypertensive patient should always include assessment of renal function.

Hemodialysis Patients: Anaphylactoid reactions have been reported in patients dialyzed with high-flux membranes (e.g., AN 69*) and treated concomitantly with an ACE inhibitor. In these patients consideration should be given to using a different type of dialysis membrane or a different class of antihypertensive agent.

Hyperkalemia: Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately one percent of hypertensive patients in clinical trials treated with enalapril alone. In most cases these were isolated values which resolved despite continued therapy, although hyperkalemia was a cause of discontinuation of therapy in 0.28 percent of hypertensive patients. Hyperkalemia was less frequent (approximately 0.1 percent) in patients treated with enalapril plus hydrochlorothiazide. Risk factors for the development of hyperkalemia include renal insufficiency, diabetes mellitus, and the concomitant use of potassium-sparing diuretics, potassium supplements and/or potassium-containing salt substitutes, which should be used cautiously, if at all, with enalapril. (See *Drug Interactions.*)

Cough: Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is nonproductive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Hydrochlorothiazide: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving thiazide therapy should be observed for clinical signs of fluid or electrolyte imbalance: hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hypokalemia may develop, especially with brisk diuresis, when severe cirrhosis is present, or after prolonged therapy. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Hypokalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Because enalapril reduces the production of aldosterone, concomitant therapy with enalapril attenuates the diuretic-induced potassium loss (see *Drug Interactions, Agents Increasing Serum Potassium*).

Although any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease), chloride replacement may be required in the treatment of metabolic alkalosis.

Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

In diabetic patients dosage adjustments of insulin or oral hypoglycemic agents may be required. Hyperglycemia may occur with thiazide diuretics. Thus latent diabetes mellitus may become manifest during thiazide therapy.

The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient.

If progressive renal impairment becomes evident consider withholding or discontinuing diuretic therapy.

Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia.

Thiazides may decrease urinary calcium excretion. Thiazides may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

Information for Patients; Angioedema: Angioedema, including laryngeal edema, may occur at any time during treatment with angiotensin converting enzyme inhibitors, including enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, extremities, eyes, lips, tongue, difficulty in swallowing or breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Hyperkalemia: Patients should be told not to use salt substitutes containing potassium without consulting their physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

Pregnancy: Female patients of childbearing age should be told about the consequences of second- and third-trimester exposure to ACE inhibitors, and they should also be told that these consequences do not appear to have resulted from intrauterine ACE-inhibitor exposure that has been limited to the first trimester. These patients should be asked to report pregnancies to their physicians as soon as possible.

NOTE: As with many other drugs, certain advice to patients being treated with VASERETIC is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions; Enalapril Maleate; Hypotension—Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. If it is necessary to continue the diuretic, provide medical supervision for at least two hours and until blood pressure has stabilized for at least an additional hour. (See WARNINGS.)

Agents Causing Renin Release: The antihypertensive effect of enalapril is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: Enalapril has been used concomitantly with beta adrenergic-blocking agents, methyldopa, nitrates, calcium-blocking agents, hydralazine and prazosin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: Enalapril attenuates diuretic-induced potassium loss. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalemia they should be used with caution and with frequent monitoring of serum potassium.

Lithium: Lithium toxicity has been reported in patients receiving lithium concomitantly with drugs which cause elimination of sodium, including ACE inhibitors. A few cases of lithium toxicity have been reported in patients receiving concomitant enalapril and lithium and were reversible upon discontinuation of both drugs. It is recommended that serum lithium levels be monitored frequently if enalapril is administered concomitantly with lithium.

Hydrochlorothiazide: When administered concurrently the following drugs may interact with thiazide diuretics:

Alcohol, barbiturates, or narcotics—potentiation of orthostatic hypotension may occur.

Antidiabetic drugs (oral agents and insulin)—dosage adjustment of the antidiabetic drug may be required.

Other antihypertensive drugs—additive effect or potentiation.

Cholestyramine and colestipol resins—Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively.

Corticosteroids, ACTH—intensified electrolyte depletion, particularly hypokalemia.

Pressor amines (e.g., norepinephrine)—possible decreased response to pressor amines but not sufficient to preclude their use.

Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)—possible increased responsiveness to the muscle relaxant.

Lithium—should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with VASERETIC.

Non-steroidal Anti-inflammatory Drugs—In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when VASERETIC and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Enalapril in combination with hydrochlorothiazide was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. Enalapril-hydrochlorothiazide did not produce DNA single strand breaks in an *in vitro* alkaline elution

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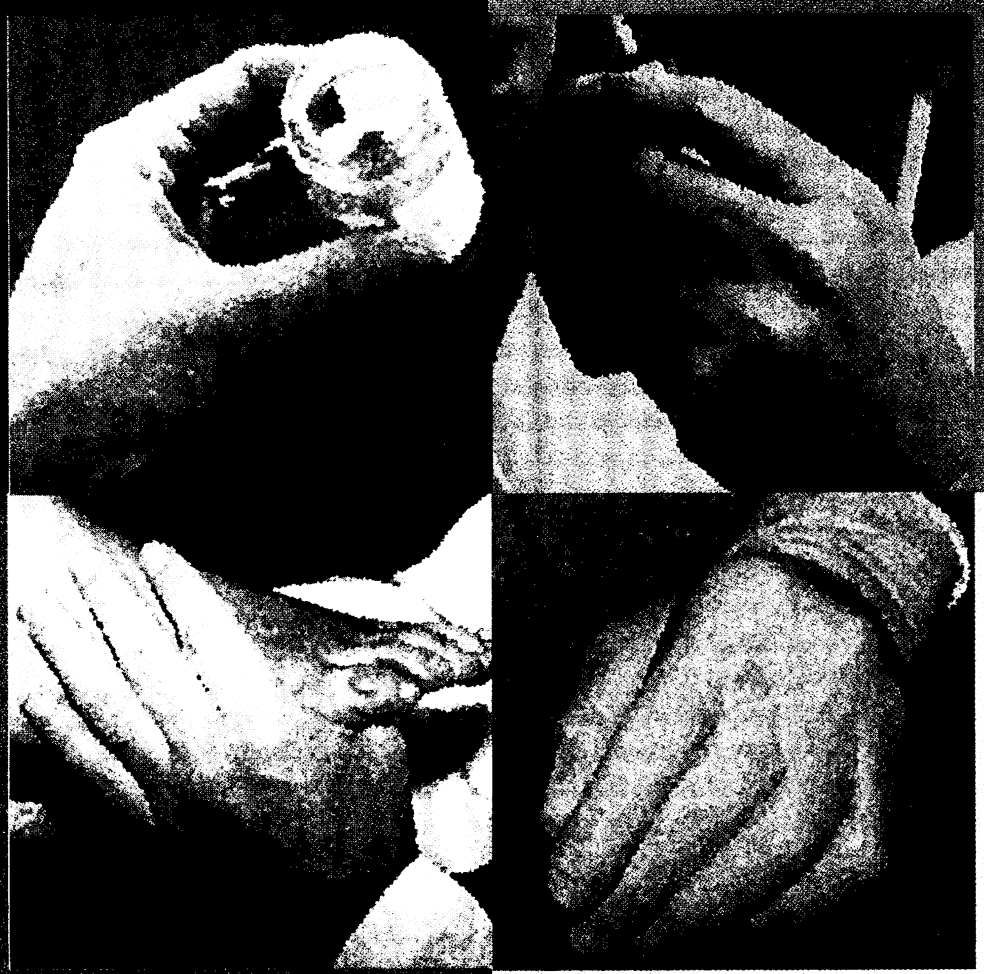
California Medical Association's Western Scientific Assembly and 123rd Annual Session

March 17-23, 1994

Disneyland Hotel, Anaheim



This FREE PROGRAM is open to all Annual Session Badge Holders

GOLDEN APPLE AWARD AND RECEPTION

"Doctor James Lind: Taking the History and Changing the History of the World"

Friday, March 18, 5:30 pm
Disneyland Hotel Convention Complex

Doctor Sherman M. Mellinkoff has been selected by the Committee on Scientific Assemblies to receive CMA's 1994 Golden Apple Award. This award spotlights exceptional physicians who have made a lifelong commitment to teaching and are renowned for their charismatic, scientific and educational talents.

Doctor Mellinkoff is Emeritus Professor of Medicine at the UCLA School of Medicine, where he served as Dean for 24 years. Following his medical education (Alpha Omega Alpha) and internship at Stanford in the mid-1940s, he served in the Army Medical Corps for two years and subsequently as Assistant, Associate and Chief Resident on the Osler Service at Johns Hopkins Hospital in Baltimore, and as Fellow in Gastroenterology at the University of Pennsylvania. In 1981 he received the Abraham Flexner Award of the Association of American Medical Colleges for his outstanding contributions to medical education.

Doctor Mellinkoff's address will explore the work of 18th century physician, James Lind, whose clinical skill changed the course of medical and world history. Between 1500 and 1800 more seamen were killed by scurvy than by all other causes. Citrus juice, Lind discovered, was a cure for scurvy, and a practical means of preventing it on long voyages. Rid of this debilitating disease, the British Navy defeated Napoleon's fleet at the Battle of Trafalgar! Correct diagnosis and treatment still rely on taking an accurate medical history. Doctor Mellinkoff will discuss the applicability of Lind's methods to modern clinical practice.

We encourage all to attend CMA's Golden Apple Award presentation and reception to help us honor this outstanding teacher.

The financial assistance of Cooperative of American Physicians, Inc. - Mutual Protection Trust is gratefully acknowledged in making this reception possible.

The Western Scientific Assembly Courses: March 17-20, 1994

CMA's 1994 Western Scientific Assembly offers an exceptional educational opportunity that meets *your needs* for clinical courses, workshops and seminars that are:

- Highest quality
- Convenient
- Practical
- Economical
- Multispecialty
- CME Approved

Primary care physicians and specialists must daily assess, evaluate, and treat patients who present with complex symptoms requiring knowledge that spans a broad range of specialties. The 1994 Western Scientific Assembly provides the most time-efficient, and cost-effective opportunity to learn the latest clinical and research developments at the largest multispecialty meeting on the West Coast!

Dozens of available courses are designed to provide you with useful, practical clinical knowledge and skills immediately applicable to your day-to-day practice needs. Courses average 3-4 hours of Category I CME credit and have also been approved for American Academy of Family Physicians prescribed credit and American College of Emergency Physicians Category I credit.

THURSDAY COURSES March 17

AM 01 Basic Cardiac Life Support

PM 02 What's Up Doc? Cartoons that Sell a Smokefree Lifestyle

03 Reducing Your Overhead and Realizing Increased Income

FRIDAY COURSES March 18

AM 04 Advanced Cardiac Life Support: Provider Course (2-day course meets Friday and Saturday)

05 Practical Neurology

06 Cost-Effective Pulmonary Medicine

07 Skin Cancer: A Clinical and Histopathologic Update

08 Pediatric Otolaryngology: What Gatekeepesr Need to Know

09 How to Improve Your Collection Results

10 GRATEFUL MED Training: Referencing the NLM Databases

PM 11 Common Neurosurgical Problems in Medical Practice

12 Emergencies in Primary Care

13 Current Issues in Dermatology

14 Cancer Detection & Follow-Up in Primary Care

15 They Can't Take That Away From Me: Medicine in Transition

SATURDAY COURSES March 19

AM 16 Advanced Cardiac Life Support: Provider Retraining
17 Pediatric Emergencies
18 Dilemmas In Women's Imaging
19 Drug & Alcohol Emergencies in Primary Care
20 New Anesthetic Agents in Ambulatory Care
21 Caring for Terminally Ill: Caring When You Can't Cure
22 Resurgence of TB: The New Face of an Old Nemesis
23 Immunologic Controversies In Private Practice
24 GRATEFUL MED Training: Referencing the NLM Databases
PM 25 Health Care Issues for Women Over 40
26 Psychiatric Emergencies in Primary Care
27 Frontiers in Nuclear Oncology
28 Practical Aspects of Occupational Medicine
29 Cultural Competence in Medical Practice
30 HIV/AIDS Essential Issues for Private Practice

SUNDAY COURSES March 20

AM 31 Urology for Primary Care Physicians
32 Multiple Views of Pain Management
33 Long Term Care Update
34 Outpatient Procedures for the Primary Care Physician
35 Future Trends in Outpatient Surgery
36 Ophthalmologist-Gatekeeper: Managed Eye Care
37 Suture Course
38 Legal Clinic on Combatting Fraud and Abuse
PM 39 Musculoskeletal Trauma in Children and Adolescents
40 Risk In Cost-Contained Care
41 No-Scalpel Vasectomy Orientation and Workshop
42 Silicone Breast Implants: Fact vs. Fiction
43 Residency Selection and Career Planning

To receive a copy of the 40-page Advance Program which provides complete objectives schedules, CME information, and registration details, please call (415) 882-3384.

This FREE PROGRAM is open to all Annual Session Badge Holders

DISTINGUISHED SPEAKER

Robert E. Rakel, MD

Sunday, March 20, 1994, 1:00 - 2:00 pm
Disneyland Hotel
Convention Complex Marina Ballroom

THE FUTURE OF GENERAL MEDICINE

Doctor Robert E. Rakel, host of "Family Practice Update" presented every Sunday on Lifetime Television, will discuss the current state of healthcare reform in the United States and the impact it will have on all physicians, especially those in primary care. Can the specialty maldistribution problem be corrected and can quality healthcare be maintained while healthcare reform focuses on lower cost? Doctor Rakel will look at the current options being proposed and offer comments on those most likely to make it through Congress.

Doctor Rakel received his MD at the University of Cincinnati, College of Medicine in 1958. Following residency training, he began his career in private practice in Newport Beach, California. Currently, Doctor Rakel serves as the Richard M. Kleberg, Sr. Professor and Chair of the Department of Family Medicine, as well as the Associate Dean for Academic And Clinical Affairs at Baylor College of Medicine in Houston, Texas. He was previously Chair of the Department of Family Medicine at the University of Iowa and the University of California, Irvine, as well as Director of the Family Practice Residency Program at Hoag Memorial Hospital in Newport Beach.

In addition, Doctor Rakel has edited several important textbooks including Textbook of Family Practice, Conn's Current Therapy, Essentials of Family Practice, and Yearbook of Family Practice. He serves on the editorial boards of Journal of the American Medical Association, The Journal of Family Practice, and Family Practice News.

We are pleased to welcome Doctor Rakel back to California this year as our Distinguished Speaker and invite all to come listen to his provocative discussion on the future of general medicine.

CMA's Western Scientific Assembly and Annual Session

CMA HOUSE OF DELEGATES

The CMA House of Delegates meets each day, Saturday, March 19 through Wednesday, March 23. House Speaker, Doctor Jack McCleary, notes that the current schedule of the House provides delegates with time to attend scientific programs, view the exhibits and participate in delegation caucuses.

Highlights of this year's House will be the farewell address of outgoing CMA President, David R. Holley, MD, a Monterey radiologist, and the inaugural address of CMA's President-Elect Ralph Ocampo, a San Diego general surgeon.

YOUNG PHYSICIANS SECTION ANNUAL ASSEMBLY

All California physicians under 40 years of age or in their first five years of practice are invited to attend the CMA Young Physicians Section (YPS) Annual Assembly which meets Friday and Saturday, March 18-19. The Assembly debates resolutions on a myriad of medical practice and health policy issues and forwards its recommendations to the CMA House of Delegates, the AMA or its own Executive Committee for action. For additional information, please contact Roger Purdy at (415) 882-5127.

CMA HOSPITAL MEDICAL STAFF SECTION ANNUAL ASSEMBLY

Medical staff leaders from throughout the state will come together at the 1994 CMA-HMSS Annual Assembly. In addition to updates on legal and legislative issues, this year's meeting will feature an educational conference on "Medical Staff Issues: 1994." For more information about the HMSS agenda, registration fees or membership, call (415) 882-5170.

EXHIBIT HALL

During the Western Scientific Assembly, the Exhibit Hall will feature exhibits for everyone: pharmaceuticals, educational displays, computer systems, office systems, insurance, investment opportunities, medical testing systems, health and home products, and much more. Admission is FREE. Be sure to alert your office managers to schedule time to visit the Exhibit Hall.

CMA ALLIANCE

Spouses of physicians can get involved at the Annual Meeting of the CMA Alliance. Board meetings are scheduled from Friday, March 18 through Sunday, March 20. The CMA-A House of Delegates meets Sunday, March 20 through Tuesday, March 22. Educational programs and a silent auction benefiting Community Health Foundation will be held on Friday and Saturday. For more information, call Patty Frisk at (415) 882-5193.

GENERAL INFORMATION

LOCATION

The CMA 1994 Western Scientific Assembly will be held at the Disneyland Hotel, 1150 West Cerritos Avenue, Anaheim, CA 92803. Call (714) 778-6600 for hotel registration information and directions.

All physicians and health professionals attending Western Scientific Assembly courses must pay general registration fees, with the exception of member medical students. Physicians and guests who do not attend any courses are not required to pay a fee. The many FREE programs include: Exhibit Hall, Golden Apple Award and Reception, a Critical Look at the Washington Scene, Distinguished Speaker, Medical Progress: A Miracle at Risk, and others.

PRE-REGISTER BY FEBRUARY 1, 1994 FOR EARLYBIRD SAVINGS

Advance registration closes February 18, after which attendees may register on site at the Disneyland Hotel's Center Lounge:

Thursday, March 17 _____7:00 am to 5:00 pm

Friday, March 18 _____7:00 am to 5:00 pm

Saturday, March 19_____7:00 am to 5:00 pm

Sunday, March20 _____7:00 am to 5:00 pm

FOR MORE INFORMATION

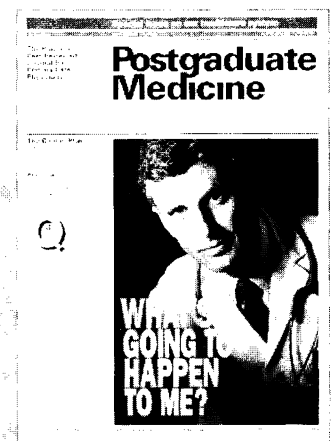
Contact CMA's Western Scientific Assembly office at (415) 882-3384.

We hear your concerns about healthcare reform. That's why Postgraduate Medicine is devoting several upcoming issues exclusively to healthcare reform. We're calling these special issues **"Healthcare '94."**

Look for the February 15th, May 15th, September 15th and November 15th issues.

Our mission is to keep you abreast of the changes that will affect primary care physicians.

"Healthcare '94." The place to find answers to your questions about healthcare reform.



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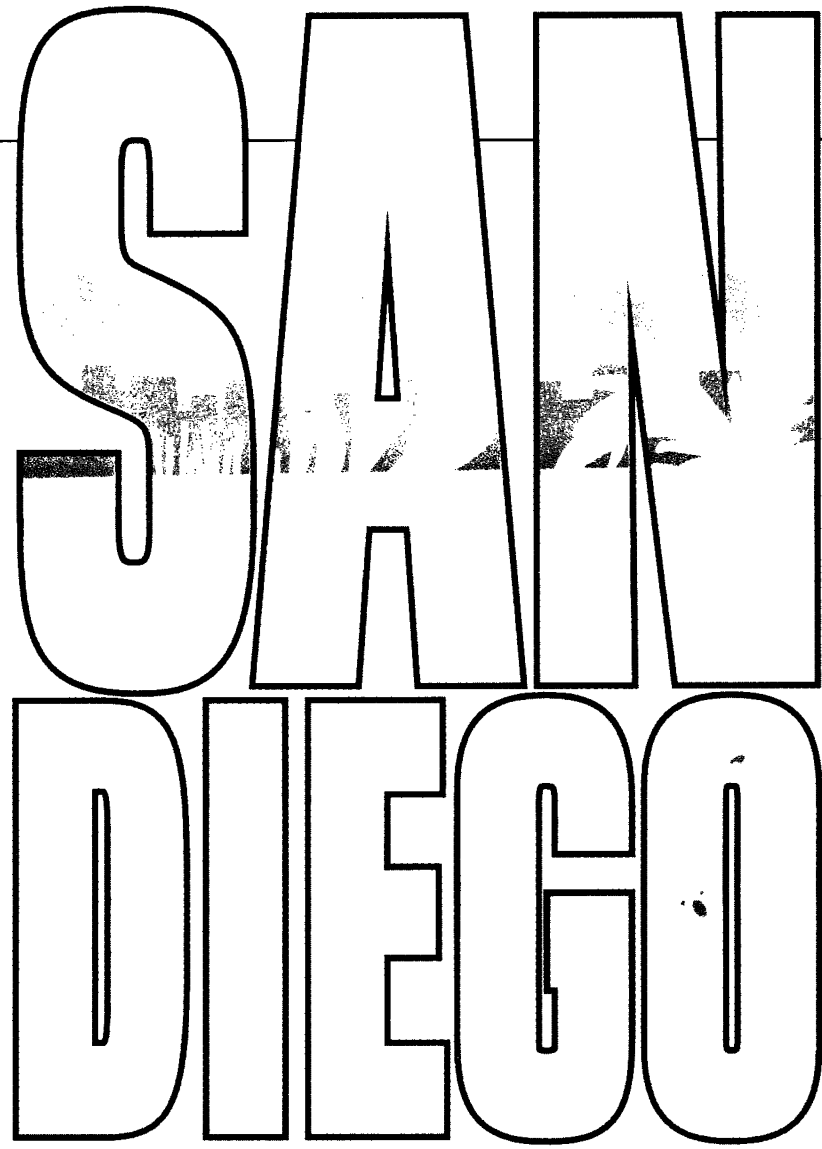

. . . for the 62nd Annual Meeting of the
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The Southern Medical Association is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

MARCH 4-6, 1994

PHYSICAL MEDICINE & REHABILITATION
LOCATION: New Orleans, Louisiana
SPECIALTY: Physical Medicine, Physiatry, Orthopaedics
CME CREDIT: AMA Category I
FEE: SMA Member $310; Nonmember $435; Nonphysician $225

MARCH 10-12, 1994

SEC SPORTS MEDICINE
LOCATION: Memphis, Tennessee
SPECIALTY: Orthopaedics, Family Practice, Sports Medicine
CME CREDIT: AMA Category I
FEE: SMA Member $250; Nonmember $400; Nonphysician $125

MARCH 10-13, 1994

GASTROENTEROLOGY UPDATE
LOCATION: Howey-in-the-Hills (Orlando), Florida
SPECIALTY: Gastroenterology, Internal Medicine
CME CREDIT: AMA Category I, 15 hours
FEE: SMA Member $375; Nonmember $500

MARCH 18-20, 1994

DEPRESSION AND ANXIETY UPDATE
LOCATION: Hilton Head, SC
SPECIALTY: Primary Care, Psychiatry
CME CREDIT: AMA Category I, 15 hours
FEE: SMA Member $310; Nonmember $435

APRIL 7-10 1994

FOCUS ON THE FEMALE PATIENT
LOCATION: Howey-in-the-Hills (Orlando), Florida
SPECIALTY: Primary Care, Ob/Gyn
CME CREDIT: AMA Category I
FEE: SMA Member $310; Nonmember $435

APRIL 15-17, 1994

ADDICTION MEDICINE
LOCATION: New Orleans, Louisiana
SPECIALTY: Primary Care, Psychiatry, Emergency Medicine
CME CREDIT: AMA Category I, 15 hours
FEE: SMA Member $350; Nonmember $475

APRIL 15-17, 1994

ORTHOPAEDIC UPDATE
LOCATION: Wrightsville Beach, NC
SPECIALTY: Orthopaedic Surgery
CME CREDIT: AMA Category I, 14 hours
FEE: SOA Member $125; SMA Member $225; Nonmember $350

APRIL 22-24, 1994

INFECTIOUS DISEASES
LOCATION: Fort Lauderdale, Florida
SPECIALTY: Primary Care
CME CREDIT: AMA Category I, 15 hours
FEE: SMA Member $310; Nonmember $435

For more information, call Michelle Williamson, Southern Medical Association, 800-423-4992 or 205-945-1840—TODAY!

PACE PROFILE

Vaughn A. Starnes, M.D. has joined the University of Southern California School of Medicine.

Vaughn A. Starnes, M.D., has joined the University of Southern California School of Medicine as Professor of Surgery, Chief of the Division of Cardiothoracic Surgery and Director of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center. Dr. Starnes is a world-recognized leader and innovator in adult and pediatric heart, heart-lung and lung transplantation and treatment of congenital heart disease.

In 1984 Dr. Starnes was accepted to the Stanford Cardiothoracic program, where he completed two years as a resident in cardiovascular surgery, and one year as chief resident in cardiac transplantation under the guidance of Norman Shumway, M.D.

In 1988 Dr. Starnes was appointed director of Stanford's heart-lung transplantation program, and later became chief of pediatric heart surgery and director of the transplant program at Stanford's Lucile Salter Packard Childrens Hospital. He performed about 400 adult and pediatric cardiac cases annually at Stanford. In addition to his adult cardiothoracic surgical expertise, Dr. Starnes earned a national reputation for his work in pediatrics.

Dr. Starnes also pioneered lung and heart-lung transplant procedures in children that previously had only been performed on adults. In 1991 he was the first surgeon to transplant the left upper lobe of a 2-year-old donor into a newborn with pulmonary hypertension who could not be weaned off ECMO (Extracorporeal Membrane Oxygenation). In 1992, he performed the first lung transplant on a baby with congenital diaphragmatic hernia.

USC Cardiothoracic Center

New Era of Excellence

The arrival of Vaughn A. Starnes, M.D., at the University of Southern California School of Medicine marks a new era of excellence in the treatment of cardiovascular disease. This commitment is exemplified in the creation of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center.

Comprehensive Services

The USC Cardiothoracic Center is one of a handful of centers in the country to provide a comprehensive range of adult and pediatric cardiovascular services including adult and pediatric heart, heart-lung and lung transplantation.

The Center features a non-invasive vascular diagnostic laboratory, diagnostic angiography laboratory and state-of-the-art cardiac catheterization laboratories. If indicated, cardiac surgeons incorporate the latest corrective surgical techniques for conditions such as ventricular and atrial arrhythmias and aortic diseases that involve aneurysms and dissections.

The Center also specializes in the treatment of infants with congenital heart defects including hypoplastic left heart syndrome, aortic valve disease, and transposition of the great vessels.

Collaboration of Specialists

At the Center, cardiologists, cardiothoracic surgeons, vascular surgeons, anesthesiologists, radiologists, interventional radiologists and allied medical professionals pool their extensive knowledge and expertise to provide patients with the full range of diagnostic and treatment alternatives.

Goal-Directed Research

As a university-based program, the Center is actively engaged in research. Specialists identify clinical problems and then seek the answer in the laboratory. Patients benefit from this link between bench and bedside, which promises to provide a better understanding of the physiology of the disease process.

Community Resource

As a vital component of the USC School of Medicine, the USC Cardiothoracic Center serves as a key educational resource for community-based and referring physicians. Physicians are encouraged to contact the Center through PACE to obtain telephone consultations, and access information regarding new patient care techniques, medications and research protocols to receive assistance with patient management concerns.

A new era is unfolding at the USC School of Medicine. We invite you to be a part of it. For more information about the USC Cardiothoracic Center, or to refer a patient, dial:
1-800-ASK-PACE (275-7223).

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‡ *In vitro* susceptibility does not necessarily imply *in vivo* efficacy.

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References: 1. Neu HC, Wilson APR, Grüneberg RN: Amoxicillin/clavulanic acid — a review of its efficacy in over 38,500 patients from 1979 to 1992. *J Chemother* 1993. In press. **2.** Data on file, SmithKline Beecham Pharmaceuticals. **3.** Wald ER, Reilly JS, Casselbrant MC, et al: Treatment of acute sinusitis in children: Augmentin® vs. cefaclor. *Postgrad Med* (special report), August/September 1984;133-136. **4.** Data from the Institutes for Microbiology Research, Franklin, Tenn. **5.** Brown R, Pinkerton R, Tuttle M: Respiratory infections in smokers. *Am Fam Physician* 1987;36:133-140. **6.** Neu HC: Contribution of beta-lactamases to bacterial resistance and mechanisms to inhibit beta-lactamases. *Am J Med* 1985;79(suppl 5B):2-12.

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THE DIVISION OF FAMILY MEDICINE AT THE UNIVERSITY OF CALIFORNIA, SAN DIEGO is seeking faculty members interested in combining clinical practice with clinical teaching. The positions will be at the Assistant Professor level, non-tenure track. The positions involve participating in a growing community-based, full spectrum Family Practice in a multicultural community with a full range of ages, socioeconomic, and health care payor systems. Opportunities for student and resident training are incorporated in the role. Candidates should be BC in Family Medicine with a strong commitment to teaching, clinical practice, and scholarship. Rank and salary, commensurate with qualifications and experience, based on UC scale. Interested candidates should send a CV and names of three references to:

UCSD
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La Jolla, CA 92093-0807

UCSD is an equal opportunity/affirmative action employer. All applications received by April 30 or thereafter until position is filled will receive thorough consideration.

PACIFIC NORTHWEST AND ROCKY MOUNTAIN/ SOUTHWEST LOCATIONS. Opportunities in Primary Care and other specialties. Urgent need for locum tenens. Benefits include malpractice, lodging, and transportation. Assignments vary in duration. Permanent placement also available. Call or write Ed Novelli at Interim Physicians, 4155 E Jewell, #1018, Denver, CO 80222; (800) 669-0718.

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HAWAII. FAMILY PRACTITIONER needed for rural Oahu. Full-time position in nonprofit community health center. Desire dedication to work in multicultural setting. Obstetric skills preferred. Send letter and CV to Puanani Kalawa. Waianae Coast Comprehensive Health Center, 86-260 Farrington Highway, Waianae, HI 96792; (808) 696-7081.

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NORTHERN CALIFORNIA RECREATION AREA. Multispecialty group has immediate opening for an Internal Medicine practitioner with a particular interest in Critical Care. Clinical activities involve full range of Internal Medicine outpatient and inpatient practice. Beautiful northern California location offers abundant recreational opportunities as well as small town living. Competitive salary and comprehensive benefit package. Please send CV to 10978 Donner Pass Rd, Truckee, CA 96161.

PHYSICIAN FOR NATIONWIDE TRAVEL. Health research organization seeks physician for National Health and Nutrition Examination Survey sponsored by the US Public Health Service. Individual will be part of a large medical team conducting health examinations in government mobile exam centers traveling to five areas of the US through mid-October 1994. Must be licensed in one state. Full-time continuous travel required. Competitive salary, paid malpractice, per diem, car, two weeks paid vacation, holidays, and health, life, dental, disability insurance offered. Call Beverly Geline, (800) 937-8281, ext 8248. Westat, Inc, Rockville, MD. EOE.

(Continued on Page 191)

(Continued from Page 190)

PHYSICIANS WANTED

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Presently recruiting for ENT, Orthopedics, Internal Medicine, Family Practice, and Hematology/Oncology. Our new outpatient clinic building provides offices for 92 providers and includes an Ambulatory Surgery Center. We are a young, aggressive group in a well-known prepaid group practice HMO organization with excellent benefits and a very reasonable call schedule. You will have a rewarding practice opportunity with ample time to enjoy San Francisco, Lake Tahoe, and all types of water/snow sports. If interested, please call or send CV to Physician Recruitment, Administration, The Permanente Medical Group, Inc, 7373 West Ln, Stockton, CA 95210; (209) 476-3229.

CALIFORNIA–SAN LUIS OBISPO AREA. Position available in Urgent Care center on the beautiful central California coast. Competitive compensation, malpractice paid. Prefer physicians with experience or residency training in Emergency Medicine or Family Practice. Send CV to Medical Director, 283 Madonna Rd, Ste B, San Luis Obispo, CA 93405.

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CALIFORNIA, OREGON, WASHINGTON. Family Practice, OB/GYN, Internal Medicine, and Pediatric opportunities. Oberto and Associates, 920 Pinecrest Terr, Box 01, Ashland, OR 97520; (503) 482-4801.

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(Continued on Page 192)

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(Continued from Page 191)

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San Jose Medical Group is an independent physician group, affiliated with Stanford University Medical Center. Our group consists of 100 full- and part-time physicians and an extended network of 400 affiliated or contracted physicians serving sixteen different locations among 1.5 million people in Santa Clara County. We are at 158 days per 1000 in commercial HMO and 848/1000 in Medicare Risk, including SNF days among over 45,000 lives. The Health Care Advisory Board has designated our multispecialty group practice the best in managed care in the United States today and we are growing to meet the demands of tomorrow.

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PHYSICIANS. The California Department of Corrections has positions available for Internal Medicine, Primary Care, General Practice, and Family Practice at the California Correctional Center at Susanville. For more information, contact Stephen O'Barr, (916) 257-2181, ext 1213. Or FAX your résumé to (916) 322-5864. EOE.

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PACIFIC NORTHWEST. Placement specialists serving northern California, Oregon, Washington. City or rural, group or solo. Internal Medicine, Family Practice, OB/GYN, O/S, Pediatrics, Allergy, and all other specialties. Barbara Stoefen, President, The O'Kane Group, 25 NW Minnesota Ave, Ste 4, Bend, OR 97701; (800) 451-0700, FAX (503) 389-5134.

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Nonprofit, community-based Primary Care clinic in Seattle, Washington, seeking Medical Director to oversee comprehensive services to predominantly Asian and Pacific Islander immigrants. Services provided include Primary Care, nutritional and health education, OB, family planning, WIC, and mental health services. Supervise MDs, midlevel providers, pharmacist, lab tech, and residents. Teaching affiliation with medical schools and residency programs established. Help clinic develop managed care program in preparation for health care reform in Washington State.

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WASHINGTON. Openings for career oriented Emergency Physicians, BC in Emergency or Primary medical specialty. Seattle metropolitan hospital with 54,000 annual visits. Excellent salary in a stable growing group. Contact Maurice Montag in care of Tammie Johnson, 8009 S 180th, Ste 103, Kent, WA 98032; (206) 575-2595.

INTERNIST–PACIFIC NORTHWEST. The Everett Clinic, a 100 plus physician multispecialty group, is seeking BC/BE Primary Care Internist to associate with 12 person department. Clinic is 25 miles north of Seattle and has four rapidly expanding satellite offices. Everett has two accredited hospitals with 217 and 257 beds. Opportunity for exceptional personal/professional lifestyle. Position offers competitive salary with excellent benefits. Position open until filled. Send CV to Al Fisk, MD, The Everett Clinic, 3901 Hoyt Ave, Everett, WA 98201.

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NORTHERN CALIFORNIA RECREATION AREA. Multispecialty group has immediate opening for a Family Practice physician. Clinical activities involve full range of Family Practice outpatient and inpatient practice. Beautiful northern California location offers abundant recreational opportunities as well as small town living. Competitive salary and comprehensive benefit package. Please send CV to 10978 Donner Pass Rd, Truckee, CA 96161.

EXCELLENT OPPORTUNITY FOR INTERNAL MEDICINE PHYSICIAN in private practice multispecialty physician group in San Francisco. Income guarantee. No investment. Forward CV to Box 263, The Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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SAN FRANCISCO BAY AREA. Palo Alto Medical Clinic, a 160 physician multispecialty group with a national reputation for excellence, seeks BC/BE residency trained Family Practice physicians. Opportunities include strong Family Practice Department at main campus site, growing Fremont satellite, new Los Altos branch, Urgent Care, and Occupational Medicine. These are exciting opportunities for energetic people to become part of an innovative health care team. Competitive salary based on experience. Excellent benefits package. Two year partnership track. Please forward letter detailing professional interests and goals and CV to George Perlstein, MD, Medical Director, Palo Alto Medical Clinic, 300 Homer Ave, Palo Alto, CA 94301.

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ATTENTION ADVERTISERS:

The deadline for classified advertising in the **April 1994** issue of WJM is **March 1.**

Call: (415) 882-3376

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PHYSICIANS WANTED

EXECUTIVE MEDICAL DIRECTOR
Industrial Medical Council
California Dept. of Industrial Relations
$8,484 per month

The Executive Medical Director is appointed by the Industrial Medical Council to plan & carry out policies on medical issues in workers' compensation; oversee contracts & projects of the Council; monitor medical evaluators; & perform other duties as required.

Applicants must possess a physician & surgeon's certificate (MD or DO) granted under Ch. 5 (commencing with Sec. 2000) of Business & Professions Code. Requires min. 4 yrs. exper. in industrial medicine, including direct treatment of occupational injuries & illnesses, & performing medical-legal evaluations. Board certification in Occupational Medicine preferred but other ABMS or AOA board certification in specialties relating to industrial injury are acceptable. Should be exper. in administrative procedures, budgeting, & supervising medical, legal & clerical staff.

Submit a letter of intent to apply, a curriculum vitae, & two letters of reference, one of which must be from your last employer to:

Dept. of Industrial Relations
Industrial Medical Council
c/o Gayle A. Walsh, D.C.
630 Fountain Ave
Pacific Grove CA 93950

California Department of Industrial Relations

For additional information call: 408-373-1003

No written test is required. The entire examination will consist of an interview. EXEMPT FROM CIVIL SERVICE STATUS.

Western States OPENINGS

Many multispecialty groups and hospitals have asked us to recruit for over 300 positions of various specialties. Both permanent and locum tenens. Send CV to **Western States Physician Services, 5627 E. Kings Canyon, Ste 156, Fresno, CA 93727, or call (800) 873-0786.**

PUGET SOUND. BC/BE Family Practitioners to affiliate with 100 plus physician multispecialty group, located 25 miles north of Seattle. Both walk-in clinic and traditional Family Practice position available. Opportunity for exceptional personal and professional lifestyle. Positions offer competitive salary with excellent benefits. Available immediately. Send CV to J. G. Finley, MD, The Everett Clinic, 3901 Hoyt Ave, Everett, WA 98201.

FAMILY PRACTICE PHYSICIAN. Full-time in a busy walk-in medical clinic. Located in Visalia, California (Tulare County). Malpractice insurance, good salary, etc. Please call (209) 627-5555 for more information.

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Leading medical providers in Arizona, Nevada, Utah, Colorado, and New Mexico have asked us to find the best available BC/BE physicians in the specialties of ORS, IM, FP, Peds, Urgent Care, OB/GYN, Psychiatry, HEM/ONC, Pulmonology, Radiology, Occ Med, ENT, GE, MED/PED, Neurology, PAs, and NPs. Top benefits, profit sharing, guarantee first two years, plus incentive pay, early shareholder. Please call CPR in Tucson (800) 658-9166, FAX (602) 322-2676 or in Phoenix (800) 657-0354; FAX (602) 433-9548.

BC/BE GENERAL INTERNIST NEEDED. Nine physician department in 27 doctor multispecialty clinic. Guaranteed salary. Excellent benefits. CV to Mike McCraley, Ogden Clinic, 4650 Harrison, Ogden, UT 84403; (800) 234-5637.

PHYSICIANS WANTED

EMERGENCY PHYSICIAN

CODY, WYOMING has a temporary 1994 summer position available for an Emergency Physician. Work in the beautiful Rocky Mountain region, located only 50 miles from Yellowstone Park. Area abundant in fishing, camping, boating, and all outdoor sports. NO STATE INCOME TAX!! For more information **call (307) 578-2488** or send CV to **Gary Bishop, Administrator, West Park Hospital, 707 Sheridan Ave, Cody, WY 82414.**

FAMILY PRACTICE. Premier multispecialty group near Portland, Oregon has two excellent opportunities for BC/BE Family Practitioners. Join one of two satellite clinics in which Family Physicians and Physician Assistants currently practice. Superb lifestyle, abundant recreational opportunities, and generous benefits package. Send CV to Karen Stanton, c/o The Vancouver Clinic, 700 NE 87th Ave, Vancouver, WA 98664.

BC/BE OB/GYN–CALIFORNIA. TDH invites comparison with other private practice opportunities. We offer guaranteed income initially and exceptional earning potential. A growing area with new businesses, our patient population is now 105,000 currently being served by two OB/GYNs. Well equipped, 112-bed hospital. Located near Sequoia National Park, Tulare offers a desirable family environment, all amenities. Beautiful homes, close to office and hospital, are reasonably priced. Good schools, abundant recreation. California license required. Contact Tulare District Hospital Physician Recruiting Office, PO Box 90112, Los Angeles, CA 90009; (800) 468-2687.

ASSOCIATE IN PEDIATRICS. Kern Medical Center, Bakersfield, California, a teaching hospital affiliated with UCLA and UCI Schools of Medicine, seeks an Associate in the Division of Pediatrics. Prerequisites include eligibility or certification by the American Board of Pediatrics, strong interest in teaching and qualifications for faculty appointment in UCLA Department of Pediatrics. Comprehensive salary and benefit package. A part-time private practice is permitted. Medical center is in central California, a mid-sized urban community with moderate cost of living. Send CV and inquiries to Navin Amin, MD, Chairman, Department of Family Practice/Pediatrics, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

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PHYSICIANS WANTED

PRIMARY CARE

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Northwest Permanente, P.C., a professional group of physicians providing medical services to 380,000 members of Kaiser Permanente in Oregon and Southwest Washington, has excellent opportunities for board certified or eligible Family Physicians and Internists. Positions are available in the Portland/Vancouver and Salem, Oregon areas and Longview, Washington.

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BC/BE ORTHOPEDIC SURGEON–CALIFORNIA. TDH invites comparison with other private practice opportunities. We offer guaranteed income initially and exceptional earning potential. A growing area with new businesses, our patient population is now 105,000, city 40,000. Well equipped, 112-bed hospital. Located near Sequoia National Park, Tulare offers a desirable family environment, all amenities. Beautiful homes, close to office and hospital, are reasonably priced. Good schools, abundant recreation. California license required. Contact Tulare District Hospital Physician Recruiting Office, PO Box 90112, Los Angeles, CA 90009; (800) 468-2687.

LOOKING FOR THE PERFECT POSITION? Place a classified advertisement under "Positions Wanted" and get noticed. Call (415) 882-3376 for details.

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COASTAL CALIFORNIA–SAN LUIS OBISPO. Family Practice and Internal Medicine, BC/BE. Join our busy Primary Care group practice. Located midway between Los Angeles and San Francisco on the central coast of California. San Luis Obispo offers a variety of cultural/recreational activities, a beautiful coastline, vineyards, and a local university. Call or send CV to Fran Coughlin, RN, MS, Ambulatory Care Services, San Luis Obispo General Hospital, Box 8113, San Luis Obispo, CA 93403-8113. Phone (805) 781-4936, FAX (805) 781-1096.

JACKSON HOLE–FAMILY PHYSICIAN. BC/BE Family Physician for an interesting Family and Tourist Medicine practice. Office in Jackson and Grand Teton National Park. Relaxed living, no crime, good schools, great outdoor opportunities. Work with Family Physician, Physician Assistant, great patients. No OB. Salary/partnership. Income not as large as the big city but great lifestyle. Enjoy it now while you work versus retiring here in 30 years when you are too old to enjoy it!! Brent Blue, MD, (307) 733-8002.

CALIFORNIA. Ambulatory Care/Family Practice–CEP is a partnership of Ambulatory Care and Emergency Medicine specialists. We currently staff nine free-standing clinics in northern, central, and southern California, and have upcoming openings for physicians specializing in Family Practice. We offer shared ownership, excellent compensation, health, and disability insurance, retirement program, and many other benefits. For more information, send CV or call John Gravette, CEP, 2101 Webster St, Ste 1050, Oakland, CA 94612; (800) 842-2619.

(Continued on Page 196)

Moving Ahead

The California Department of Corrections with 27 locations statewide has a number of opportunities available in the following areas:

PHYSICIANS

Internal Medicine - Primary Care - General Practice - Family Practice
(Two Facilities in Blythe)
Ironwood State Prison and Chuckawalla Valley State Prison

Other openings exist at:
Calipatria, Wasco, Pelican Bay, Vacaville, Madera, and Susanville.

HIV Physicians
California Women's Facility at Madera
California Medical Facility at Vacaville

PSYCHIATRISTS

Staff Psychiatrist

Vacaville, San Luis Obispo, Chino, Soledad/Monterey, Madera, Corcoran, Delano, Ione, Wasco, Calipatria and Solano.

GOOD NEWS!! New legislation allows for Safety Retirement Package. Call for additional information.

Contact: **Anne Perez** (916) 327-7081. Send or fax CV to:

California Department of Corrections
Dept. DHCS, P.O. Box 942883, Sacramento, CA 94283-0001.
Fax (916) 322-5864 EOE.

For a Personal Interview, see us at Booth #717 at the CMA's Annual Session and Western Scientific Assembly

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PHYSICIANS WANTED

FAMILY PRACTICE RESIDENCY. FULL-TIME FACULTY POSITION. University of Wyoming, Family Practice Residency Program-Casper. This outstanding rural Family Practice residency program seeks a physician scholar to join our faculty. The program has nine faculty members, 24 residents, and a competent support staff. The residency is affiliated with the Wyoming Medical Center, the referral hospital for the state, and the program is housed in an outstanding, freestanding facility. Responsibilities include resident supervision in ambulatory and inpatient settings, participation in scholarly activities, faculty development, and direct patient care. Requirements include BC in Family Practice, ability to obtain Family Practice credentials including Obstetrics, and a strong desire to teach rural Family Practice. Completion of a teaching fellowship in Family Practice and experience with Area Health Education Centers are highly desirable. Applications should include a current CV and three references. Academic rank in based on the individual's experience, and a competitive salary and benefits are offered. The community of Casper and the state of Wyoming can provide an enjoyable life-style which is unequaled elsewhere. The University of Wyoming is an equal opportunity/affirmative action employer. Please contact Joe K. Schoeber, MD, Program Director, University of Wyoming, Family Practice Residency Program-Casper, 1522 East "A" St, Casper, WY 82601; (307) 266-3076.

FIND THE RIGHT PHYSICIAN FOR YOUR PRACTICE. Place a Classified Ad in The Western Journal of Medicine. For more information, or to request a media kit, call (415) 882-3376.

PHYSICIANS WANTED

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TWO INVASIVE CARDIOLOGISTS AND FAMILY PHYSICIANS NEEDED. Unique opportunity. Gorgeous California central coast. Partnership within year. Send references/CV to Number 286, The Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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Highly respected, 35 member multispecialty group seeks second Medical Oncologist to join a busy, regional practice. Group is site for CCOP protocols and practices out of one of Oregon's premier hospitals. Portland offers an outstanding quality of life near mountains and the ocean. **Call Martin Osinski; (800) 327-1585.**

SPLASH? HAWAII, CALIFORNIA, ARIZONA clinics need Family Practitioners, Internists, and OBs. Benefits. Clear speech. CVs to LAM Associates, Dept W, 444 Hobron Ln, #207H, Honolulu, HI 96815-1229; Pat Lam, (808) 947-9815, 10 am-8 pm PST.

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MEDICAL GROUP ADMINISTRATOR/BUSINESS MANAGER desires position with small/medium single specialty physician group. Five years experience in all phases of management: Personnel, accounts receivable/payable, insurance, etc. Salary negotiable. Reply: J. Bowman, PO Box 1004, Lawrenceville, GA 30246-1004. Phone (404) 682-0518.

INDUSTRIAL MEDICINE. Experienced, energetic, surgical specialty boarded MD seeks full-time position in San Francisco Bay area. Respected by workers and management for objective approach. Superb results in conservative care of repetitive stress injuries at major industrial plant. Excellent references, no malpractice history. Contact Box Number 290, The Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

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ATTENTION ADVERTISERS:
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Call: (415) 882-3376

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LOCUM TENENS

OFFICE SPACE

YOUR FAMILY MEDICAL GROUP, located in Anaheim, Garden Grove, and Fountain Valley, has excellent office space available to physicians on a time-sharing or sublet basis. Please contact A. Raymon, Administrator, (714) 638-8650.

PATENTS

MEDICAL DEVICES and procedures a specialty. Consult a registered patent attorney before you publish or practice your invention. Acronational Patent Law Firm, One Market Plaza, Spear Street Tower, Ste 900, San Francisco, CA 94105; (415) 777-9017.

PRACTICES AVAILABLE

PHYSICIAN IN GENERAL PRACTICE wishes to retire. Looking for doctor to take over practice, office staff, and rent his building. Call (209) 674-4717. In growing town of central San Joaquin Valley.

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PAIN TREATMENT CENTER FOR SALE. Established 1977. San Diego County. Fully equipped and furnished. All private pay. Available to stay for introduction. Suitable for Orthopedist, Neuropsychiatrist, Physiatrist. Contact K. Shandell, MD, 2225 Camino del Rio South, Ste B, San Diego, CA 92108.

CALIFORNIA, LANCASTER. Retiring Family Practitioner, 32 years established practice in rapidly growing area, desires physician to take over practice, staff, and assume office lease in new building near three hospitals. Office is fully equipped and operational with its own laboratory and x-ray. (805) 942-3983 (message).

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PHYSICIANS–Advertise your positions available, office space, practice available, or vacation home in WJM classifieds. Call (415) 882-3376 for details.

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MEDICAL LITERATURE RESEARCH. Physician/educator/editor will do customized literature searching and analysis for medical or legal problems. Call Bill Milburn, MD, (303) 823-5083.

CONFERENCES

SEVENTH CHARLESTON SYMPOSIUM ON CONGENITAL HEART DISEASE. March 10-12, 1994. Charleston, South Carolina. Fees: $495 for ACC members; $560 for non-members; $220 for fellows-in-training, residents, nurses, physician assistants, and technologists. 15.5 Category 1 credit hours. For information, call American College of Cardiology, (800) 257-4739, FAX (301) 897-9745.

CARDIOLOGY FIESTA in San Antonio. Update on cardiac diagnostic and therapeutic techniques. April 21-23, 1994. San Antonio, Texas. Fees: $395 for ACC members; $465 for non-members; $250 for fellows-in-training, residents, nurses, physician assistants, and technologists. 17.5 Category 1 credit hours. For information, call American College of Cardiology, (800) 257-4739, FAX (301) 897-9745.

SEVENTH ANNUAL STATE-OF-THE-ART ECHO-CARDIOGRAPHY. February 17-20, 1994. Tucson, Arizona. Fees: $525 for ACC members; $610 for non-members; $415 for fellows-in-training, residents, nurses, physician assistants, and technologists. 24 Category 1 credit hours. For information, call American College of Cardiology, (800) 257-4739; FAX (301) 897-9745.

CONFERENCES

NINTH ANNUAL CARDIOVASCULAR CONFERENCE AT HAWAII. February 14-18, 1994. Hyatt Regency Waikoloa, Kohala Coast, Hawaii. Fees: $450 for ACC members; $545 for non-members; $270 for fellows-in-training, residents, nurses, physician assistants, and technologists. 20.5 Category 1 credit hours. For information, call American College of Cardiology, (800) 257-4739; FAX (301) 897-9745.

CARDIOVASCULAR CONFERENCE AT LAKE LOUISE. February 28-March 3, 1994. Lake Louise, Alberta, Canada. Fees: $410 for ACC members; $495 for non-members; $250 for fellows-in-training, residents, nurses, physician assistants, and technologists. 17.5 Category 1 credit hours. For information, call American College of Cardiology, (800) 257-4739; FAX (301) 897-9745.

TWELFTH ANNUAL ARCTIC MEDICAL SEMINAR at Plummer's Great Slave Lake Lodge, Canada's Northwest Territories–July 23-30, 1994. Topics in contemporary medicine. All specialties. Approved 25 CME credits, category 1. Sponsored by North Memorial Medical Center, Minneapolis, Minnesota. Contact (612) 588-9478.

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Reference: 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

PRAVACHOL® (Pravastatin Sodium Tablets)

CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

Pregnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

WARNINGS

Liver Enzymes: HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

PRECAUTIONS

General: Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

Homozygous Familial Hypercholesterolemia. Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

Renal Insufficiency. A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3α-hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life ($t_{1/2}$) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

Information for Patients: Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Drug Interactions: *Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin:* See WARNINGS: Skeletal Muscle.

Antipyrine: Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

Cholestyramine/Colestipol: Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

Warfarin: In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and Cmax of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

Cimetidine: The $AUC_{0\text{-}12hr}$ for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

Digoxin: In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

Gemfibrozil: In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, Cmax, and Tmax for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with *aspirin, antacids* [1 hour prior to PRAVACHOL (pravastatin sodium)], *cimetidine, nicotinic acid,* or *probucol,* no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

Other Drugs: During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

Endocrine Function: HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced ($p<0.004$) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a ≥50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

CNS Toxicity: CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose ($p<0.01$). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls ($p<0.05$). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli;* a forward mutation assay in L5178Y TK +/− mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae.* In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area ($mg/meter^2$). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

Nursing Mothers: A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: **General**.)

ADVERSE REACTIONS

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug:

	All Events %		Events Attributed to Study Drug %	
Body System/Event	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

Skeletal: myopathy, rhabdomyolysis.

Neurological: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematous-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal: pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma; anorexia, vomiting.

Reproductive: gynecomastia, loss of libido, erectile dysfunction.

Eye: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Test Abnormalities: Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

Concomitant Therapy: Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: **Skeletal Muscle** and PRECAUTIONS: **Drug Interactions.**)

OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.

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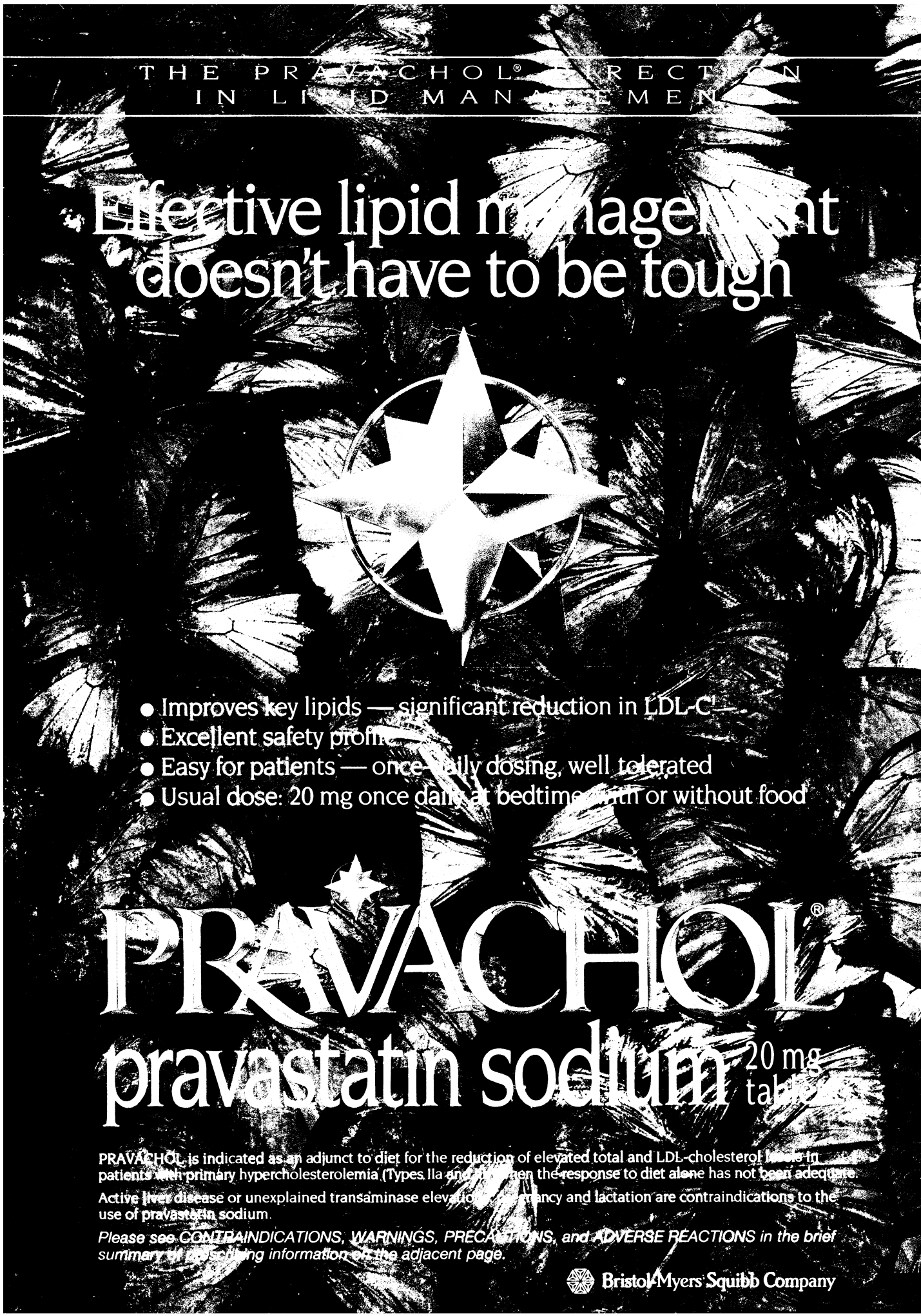
THE PRAVACHOL® DIRECTION
IN LIPID MANAGEMENT
Effective lipid management doesn't have to be tough
• Improves key lipids — significant reduction in LDL-C
• Excellent safety profile
• Easy for patients — once-daily dosing, well tolerated
• Usual dose: 20 mg once daily at bedtime with or without food
PRAVACHOL®
pravastatin sodium
20 mg tablets
PRAVACHOL is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate.
Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin sodium.
Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.
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